The Cornell-Bahia Program, 1975-1978.
The Development of a Tropical Communicable Diseases Center*

D. L. Gibbs, W. D. Johnson, Jr., T. C. Jones and
A. G. Baptista

Cornell University Medical College, New York, N.Y.;
The Federal University of Bahia, and the Fundacao
Goncalo Moniz, Salvador, Bahia, Brazil.

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Address reprint requests to Dr. Warren D. Johnson, Jr.,
Infectious Diseases Division, Department of Medicine,
Cornell University Medical College, New York, N.Y., 10021.

In 1975, Cornell University Medical College, the Federal University of Bahia, and the State of Bahia initiated a cooperative international program to develop a center for the study and control of communicable diseases in northeastern Brazil. The objectives of the program were to develop a reference laboratory to support the local health facilities, to provide laboratory support for community public health programs, to train Brazilian personnel in clinical microbiology, and to develop links between this laboratory and research or clinical activities within the University of Bahia. The program included a limited exchange of health professionals and students from the two Universities and the State of Bahia. The anticipated benefit to Bahia included access to educational opportunities, the availability of a reliable microbiology laboratory, and the introduction of new techniques and equipment for research. Cornell University would benefit by having access to a Communicable Diseases Center for the training of its medical students, fellows and faculty in clinical tropical medicine, as well as having a center for tropical disease research. This report describes the development of the laboratory, the training of personnel, and a preliminary assessment of the program.

Development of the Communicable Diseases Center.

This program evolved from a previous collaborative program of training and research between Cornell University Medical College and the University of Bahia (1). This former program was initiated

in 1964 with the support of the Commonwealth Fund of New York. Twenty-three Brazilian physicians spent six months to three and one-half years working or training at Cornell under the auspices of this program. Eleven Cornell faculty members and 34 senior medical students worked and studied in Bahia. The program had fulfilled the expectations of the partners and provided the necessary base for the development of a unique entity in the Northeast of Brazil.

In addition to these institutional and personal ties, Bahia was geographically well suited as a site for a tropical Communicable Diseases Center. Salvador, the capital of the State of Bahia, has a population of over 1.3 million and is located on a peninsula just south of the equator. Although the city is a metropolitan center in many respects, it is suffering from the burden of rapid growth. The city's population has tripled in the past 25 years and one-half of the economically active population is unemployed or underemployed (2). Less than 10% of Salvador's residences are connected to a central sewage system. Diarrheal illness is common and is reflected in the infant mortality rate which exceeds 10%. Most of the major communicable diseases of the world are prevalent within the State of Bahia, including schistosomiasis, leprosy, leishmaniasis (visceral and mucocutaneous), typhoid fever, Chagas' disease, hepatitis, polio, diphtheria, tuberculosis, and leptospirosis.

The planning period for the Communicable Diseases Center coincided with the implementation of a Rockefeller Foundation

experiment designed to enhance community development through University of Bahia programs. A number of University disciplines were to be strengthened including agriculture, marine biology, economics and public health with the expectation that the community would benefit from this new expertise. Since the objectives of our proposed Communicable Diseases Center were consistent with the Foundation's interests, they provided the funding necessary to initiate our program.

The site chosen for the Communicable Diseases Center was the State's Fundacao Goncalo Moniz which occupied one-fourth of an acre in the center of Salvador and was located two blocks from the University of Bahia Medical School. The Fundacao was established in 1915, and had a long tradition of research and service. It had previously housed the laboratories of Hideyo Noguchi (3). Two of the six buildings were to be renovated and converted into microbiology laboratories. A University of Bahia faculty member (AGB) was appointed Director of the Fundacao and coordinator of the program on behalf of the University and the State of Bahia. A Cornell faculty member was appointed to coordinate that University's input into the program.

The State of Bahia and the Federal Ministry of Health initially allocated $200,000 for building construction and renovation and an additional $103,000 for equipment which could be purchased within Brazil. The design of the laboratories and the selection of equipment was undertaken by a committee of six people representing both Universities and the State of Bahia.

Cornell University received a three year grant (1976-1979) from the Rockefeller Foundation for the purchase of imported equipment, travel, books and journals, and laboratory supplies. Cornell faculty were also eligible to receive salary support from this grant commensurate with the time they spent working in Brazil. Brazilians working in the Communicable Diseases Center were salaried by the State with several individuals also receiving compensation from the University of Bahia. The Rockefeller Foundation also provided fellowships for two Brazilians to train in clinical microbiology and immunology at Cornell. The disbursement and sources of funding for the three year period 1975-1978 are shown in Table 1.

The structural renovation of the two laboratory buildings required one year and was largely completed by January, 1977, when the first two Cornell faculty members arrived to work in Bahia. Most of the local purchase and imported equipment was also received by this time. A major problem was encountered, however, in that the buildings had been improperly wired so that large centrifuges, incubators, air conditioners, freezers, autoclaves, scintillation counters and electrophoresis apparatus could not be operated. A second electrical renovation project, requiring 16 months and $30,000, was finally completed in April, 1978. Although several planned research projects could not be initiated, the laboratory was functioning reasonably well during this period as a result of the ingenuity of several of the foreign and local staff and a considerable amount of Brazilian "jeito" (4).

Another major problem was the establishment of reliable supply lines. Routine laboratory supplies ordered through the State required at least six months to arrive. This was the result of bureaucratic delays, frequent changes in the supply budget, and the necessity of importing a majority of the microbiological materials. The laboratory could order items costing less than $250 directly from the Brazilian supplier and anticipate receipt within one month if the materials were in stock. The practical solution of this problem was the creation of a stock room system. None the less, it was still necessary to order approximately 20% of the supplies through Cornell University and hand-carry the items to Brazil by Cornell faculty or visitors. Direct shipment of items from the United States was not practical due to the long delay required for government import permits and import taxes which ranged from 100% to 1000% of the purchase price. The importation regulation also applied to State purchases.

International communications relied on air mail and telephone. Letters took five to ten days if sent air mail but up to twelve weeks if sent by regular mail. Telephone service between New York and Bahia is excellent and cheaper than telegrams. Mail and telephone service within Brazil is usually efficient but delays are not unusual.

Training Programs

The training of laboratory technicians and other health professionals was given the highest priority after laboratory renovations were completed. In Brazil, technical personnel

receive their training in University schools of pharmacy. Their curriculum is almost totally didactic and there are no standard licensing examinations. It was, therefore, necessary to create new courses which would stress laboratory methods and fundamentals of clinical microbiology. The Cornell faculty members utilized their expertise in immunology and microbiology to design such courses. The first students were technicians employed by the State but subsequent courses were offered to nurses, rural health workers, medical students and physicians (Table II). These "students" were from the University of Bahia and other institutions in the State, as well as from the States of Paraiba, Sergipe, Piaui, Alagoas, and the Federal District (Brasilia). The courses were taught by faculty of the Universities of Bahia, Sao Paulo, Rio de Janeiro, and Cornell. The mycology course was given by a consultant from the Center for Disease Control (Atlanta, Georgia). Manuals from the CDC (5-7), Mayo Clinic, University of Washington, and Cornell University were translated into Portuguese and modified for these courses. The duration of the six courses offered ranged from two to twenty weeks with several of the courses offered multiple times (Table II). The total number of course participants during 1977 and 1978 was 331.

Special fellowships for training outside Bahia were also obtained. Six technicians received six month fellowships from the Brazilian government for laboratory training at the Adolpho Lutz Institute in Sao Paulo. The Rockefeller Foundation provided fellowships (18-24 months) for three Brazilian physicians

to train in clinical microbiology and immunology at the New York Hospital-Cornell Medical Center. Arrangements were also made for a Brazilian microbiology technician to receive advanced training at the University of Colorado.

Clinical Laboratory Services

The State of Bahia had maintained a clinical microbiology laboratory at the Fundacao Goncalo Moniz for many years. However, the laboratory had not been very active recently because of inadequate funding and a general lack of interest. The laboratory performed only a few procedures, received few specimens, lacked quality control programs, and did not employ the most modern and reliable procedures available. The major source of specimens were city and state hospitals and clinics which lacked microbiology laboratories. The immediate goal was to upgrade and quality control the tests being offered and then to introduce new procedures in conjunction with our training programs. There were a number of basic tests which were not offered by any laboratories in the State. Other tests were available in several private laboratories but at a cost which was prohibitive for most patients.

Internal quality control was required since external controls were not available in Brazil. A number of simple, but fundamental, measures had a major impact on the reliability of existing procedures. Several of these initial problems and their solutions are listed in Table III. For example, the laboratory rarely isolated group A beta hemolytic streptococci from throat cultures because they utilized glucose-containing

media which inhibits hemolysis. The deletion of glucose from the media resulted in a marked increase in the number of cultures reported positive. Perhaps the best example of the value of quality control was the revision of procedures used for determining the virulence of Corynebacterium diphtheriae isolates. The laboratory processed 700 to 900 cultures per year for C. diphtheriae, of which 11% were positive. However, prior to 1977, none of the isolates were determined to be virulent by toxigenicity testing and therefore epidemiologic investigation of families and contacts was not undertaken. In 1977, the virulence testing procedure was modified and positive and negative controls were employed (8,9). Subsequently, 10% of all C. diphtheriae isolates were shown to be toxigenic. This data prompted the epidemiologic section of the State Health Department to expand their immunization and surveillance programs. A number of other tests were similarly upgraded so that reliable results were obtained (Table IV).

New procedures and tests were also introduced in 1977 and 1978 (Table IV). One example is the FTA-ABS test to confirm the diagnosis of syphilis. This test was negative in 9% of the 355 patients with positive VDRL's in 1978. This high incidence of false-positive VDRL's was due, in part, to other infectious diseases in Bahia, such as leprosy, malaria, and Chagas' disease.

The indirect hemagglutination (IHT) and fluorescent antibody (FAT) tests for Chagas' disease were also introduced in 1978. The laboratory had previously relied on the complement fixation test (CFT). The CFT lacks sensitivity and specificity (10,11).

The FAT is the first test to become positive in Chagas' disease and remains positive longer than either the IHT or CFT (12, 13). The major advantage of the IHT is its simplicity and value in screening large numbers of sera. The procedure now followed in the laboratory is to perform both the CFT and IHT on all test sera and, if only one of these two tests is positive, to confirm the diagnosis with the FAT (12). The FAT is not performed if both the IHT and CFT are positive. This procedure provides maximum sensitivity and specificity despite known cross-reactions between trypanosomal and leishmanial antigens. During a five month period, serologic tests for Chagas' disease were performed on sera from 435 asymptomatic subjects as part of routine pre-employment examinations. The CFT and IHT were not in agreement (only one positive) in 43 patients. Using the FAT as the definitive test, it was determined that the CFT yielded seven false-positive and four false-negative tests and the IHT yielded nine false-positives and 23 false-negative tests. The significant percentage of false-positive tests is of particular concern since a serologic diagnosis of Chagas' disease, even in the absence of clinical disease, makes a person ineligible for most job opportunities in Bahia.

Additional laboratory examinations introduced included serologic tests for leptospirosis, toxoplasmosis, polio and rubella (Table IV). Bacteriologic culture procedures were improved and cultures for M. tuberculosis and N. gonorrhoeae were made available. During a four month period, 16% of 256 gonococcal cultures from two health clinics were positive. The patients

were predominantly female and 90% of infected patients were asymptomatic. In addition, the laboratory now has the capability to culture enteroviruses, E. histolytica and fungi causing systemic mycoses. The confidence of the medical community in the services provided and the introduction of new examinations are reflected in the marked increase in the number of specimens received by the laboratory (Figure I). The total number of specimens received per quarter increased 5.3-fold between July, 1976, and July, 1978.

The Communicable Diseases Center has also provided support for several major public health programs. The laboratory has performed over 13,000 serologic screening tests for Chagas' disease as part of a government epidemiologic survey. The laboratory has supported several clinical studies of diarrheal illness, including a search for the enteric pathogen Vibrio parahaemolyticus. Counter immunoelectrophoresis has been used to detect bacterial antigens in the spinal fluid. This will be valuable in making specific etiologic diagnoses in partially treated meningitis patients and will be used to monitor the efficacy of the recent meningococcal immunization program completed in Brazil.

During the past year, studies of the epidemiology, pathogenesis and immunology of Chagas' disease, leprosy, and leishmaniasis have been initiated. The research program is multidisciplinary and involves investigators from the University of Bahia, Cornell University and Rockefeller University. This collaborative effort is planned as a long-term program which will yield new insights into these major diseases.

Discussion

A Communicable Diseases Center has been established in Salvador, Brazil. This facility serves as a reference laboratory for the entire State and provides support for community public health programs. The prerequisites for the successful development of such a facility include recognition of need, administrative cooperation, affiliation with universities or other sources of expertise, and patience in dealing with unavoidable problems and delays.

The need for a reliable microbiologic laboratory has been recognized for many years by the academic, clinical and administrative leaders in Bahia. Despite the importance of communicable diseases in the area, the development of clinical microbiology has lagged behind clinical chemistry and hematology. The State of Bahia is not unique in this regard. Carvalho (14, 15) recently assessed the status of public health laboratories in Brazil and made the following observations: 1) less than 1/3 of the states in Brazil have even minimally adequate central laboratory facilities; 2) the existing laboratories lack basic equipment and trained personnel; 3) microbiology-communicable diseases services have the greatest need for development; 4) regional laboratory networks were either absent or, if present, lacked adequate communications and methods for the transport of specimens. Our immediate goal to develop a central laboratory facility with a trained staff and adequate equipment has been realized. Efforts are now underway to expand and upgrade a

regional network of at least twelve laboratories throughout the State. Personnel to staff these facilities are being trained at the Communicable Diseases Center and transport systems for microbiologic materials have already been developed (16).

The development of the laboratory was facilitated by the support given the project by senior officials of the State government and the University of Bahia. These people were interested and accessible, and implemented the recommendations of the "consultants". Many unanticipated problems were encountered. Some problems were related to the lack of trained supervisory personnel and the absence of laboratory models in the area which could be emulated. Adequate communications and supply channels were eventually established by understanding the Brazilian system, enlisting the cooperation of many people, and relying on the concept of jeito (4) as the last resort (loosely translated, jeito means "a way").

University affiliations were essential to the development of the laboratory. The university is usually the only source of expertise available and also provides an invaluable stimulus for excellence. The prestige of a university affiliation can be very important to a new facility. The university also adds a new dimension to the laboratory by providing opportunities for collaborative scientific studies. The laboratory, in turn, provides the university with research facilities and clinical material related to the major health problems of the region.

The impact of this program on the study and control of communicable diseases in northeastern Brazil may not be known for many years. Emphasis in 1979 has shifted from establishing basic services to increasing utilization of the laboratory by expanding the base for referral of routine and reference specimens. The quality of health care has been improved by providing reliable laboratory support. The persons trained at the Communicable Diseases Center are also a valuable resource which should geometrically increase as they train others. The laboratory is becoming a research center with the participation of local and foreign scientists. The availability of modern laboratories, a trained technical staff, and collaborating local and foreign scientists working in a region in which the major communicable diseases of the world are prevalent provides a unique opportunity to increase our understanding of these diseases.

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Figure I. Number of clinical specimens received by the Communicable Diseases Center.

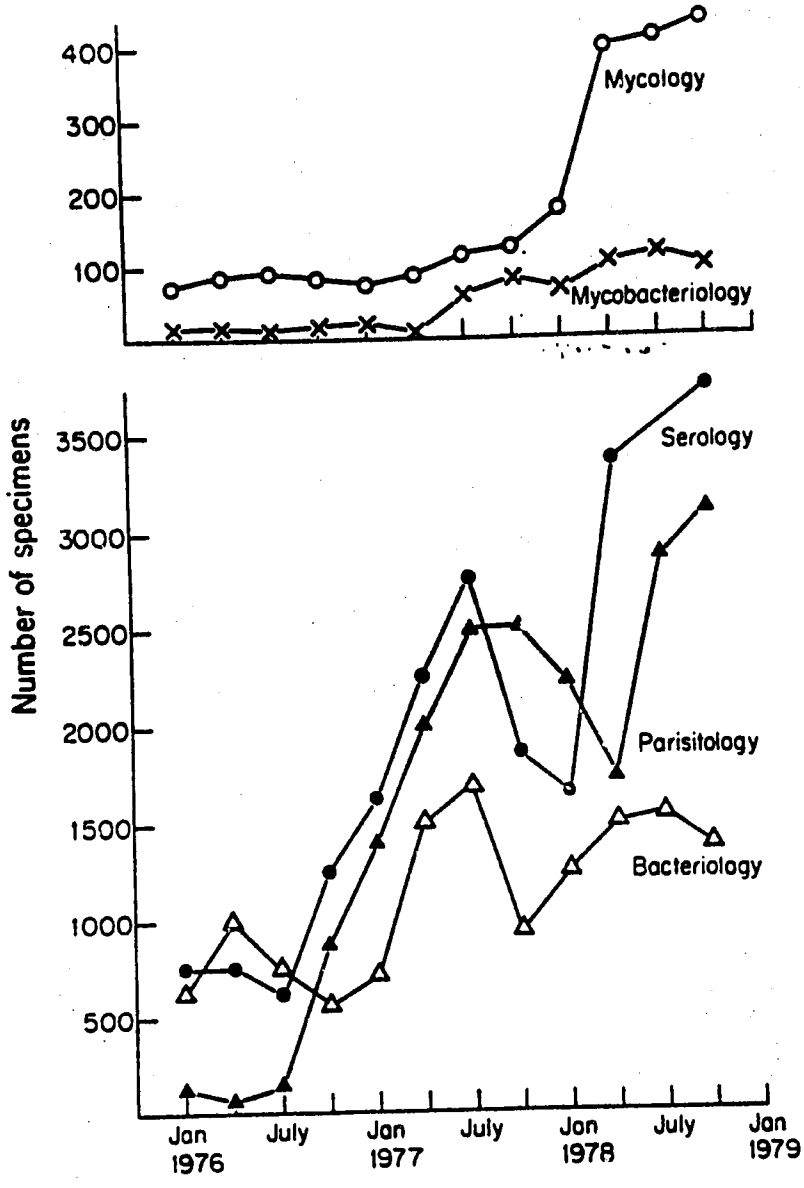

Table I. Disbursement and Sources of Funds for the Communicable Diseases Center, 1975-1978*

	State of Bahia	Brazilian Federal Government	University of Bahia	Rockefeller Foundation
Personnel	$337,493		$ 50,278	$ 44,325**
Supplies & Equipment	322,714	$ 57,003	105,000†	22,637
Renovation & Construction	332,342			
Transportation				27,303+
Housing & Per Diem				28,918‡
Miscellaneous				5,633
	$992,549	$ 57,003	$155,278	$128,816

* Sums are approximated due to changes in the dollar-cruzeiro exchange rate.

** An additional $75,000 was provided by the Rockefeller Foundation for fellowship stipends.

† These funds were provided to the University of Bahia by the Rockefeller Foundation.

+ This includes purchase and maintenance of a vehicle in Bahia and air travel by Cornell and University of Bahia personnel.

‡ This includes furnishing and maintenance of an apartment for Cornell personnel in Bahia.

Table 11 Biomedical courses offered by the Communicable Diseases Center in 1977-1978

Course Title	Lecture	Lab	Times Offered	Duration of Course weeks	hrs/week	Course Participants (Total) physicians	nurses	medical students	lab techs	rural health workers
Clinical microbiology*	X		5	2	20	33		25	60	
Basic laboratory fundamentals of microbiology	X	X	2	16	40					27
Advanced laboratory fundamentals of microbiology		X	1	12	20				96	
Advanced public health*	X		2	20	40	12	30		32	
Clinical mycology	X	X	1	4	20	1		1	5	
Basic immunology	X	X	2	4	20	5			4	
						51	30	26	197	27

* Course also included students from the States of Paraiba, Sergipe, Piaui, Alagoas, and the Federal District (Brasilia).

Table III Initial problems affecting quality of laboratory tests.

	Problem	Solution
1.	irregular electrical supply to refrigerators and incubators	daily temperature checked and emergency generator installed
2.	contaminated media	autoclave function tested; sterile technique reviewed; media room remodeled
3.	false identification of enteric bacteria	positive and negative controls utilized
4.	antibiograms unreliable	only antibiotic disks of known concentration used; strict Kirby-Bauer technique employed
5.	group A streptococci not isolated	media changed from glucose-containing to glucose-free
6.	protozoa cultures frequently contaminated	fresh antibiotic solutions used
7.	mold on microscope lens	constructed plastic boxes with silica gel dessicant to house microscopes

Table IV. The availability and reliability of tests at the Communicable Diseases Center

TESTS	YEAR		
	1976	1977	1978
Serology			
Chagas' complement fixation	U*	R	R+
hemagglutination	-	-	R
immunofluorescence	-	-	R
VDRL	-	R	R
FTA-ABS (syphilis)	-	-	R
pregnancy test	-	R	R
antistreptolysin O	R	R	R
rheumatoid factor	R	R	R
widel H and O agglutinins	R	R	R
Paul Bunnell heterophile	R	R	R
C-reactive protein	R	R	R
toxoplasma IFA	-	-	R
leptospira agglutination	-	-	R
polio complement fixation	-	-	R
rubella IHA	-	-	R
hepatitis antigen			
Bacteriology			
blood culture	U	R	R
urine culture (quantitative)	U	R	R
stool culture	U	R	R
throat culture	U	R	R
cultures of water (coliform & cholera)	R	R	R
gonococcal cultures	-	-	R
antibiograms	U	U	R
acid-fast smears (*M. tuberculosis*)	R	R	R
culture and sensitivity of *M. tuberculosis*	-	-	R
Virology			
enterovirus cultures (polio)*	-	-	R
Mycology			
dermatophytes	R	R	R
deep mycoses	-	-	R
Protozoa and Helminths			
stool O and P	R	R	R
E. histolytica cultures	-	-	R
trichomonas wet mounts & cultures	-	R	R
blood and marrow smears and cultures for protozoa	-	R	R

* U means available but unreliable
\+ R means available and reliable